

CLAIMS

1. A mutant pro-neurotrophin for use in intracellular processing of a corresponding growth factor having improved secretion efficiency as compared to a wild-type growth factor, wherein the wild-type pro-neurotrophin has an asparagine residue at a position 8 amino acids upstream from the site of cleavage for the mature growth factor, the mutant pro-neurotrophin comprising a polypeptide in which the wild-type asparagine residue is replaced by a basic residue.
2. The mutant pro-neurotrophin according to Claim 1, wherein the basic residue is serine.
3. The mutant pro-neurotrophin according to Claim 1, wherein the corresponding growth factor is selected from the group consisting of neurotrophins NGF, NT-3 and BDNF.
4. The mutant pro-neurotrophin according to Claim 1, wherein the polypeptide is a recombinant one, and the replacement of the wild-type asparagine is made by mutation of a polynucleotide encoding the wild-type pro-neurotrophin.
5. A mutant pro-neurotrophin for use in intracellular processing of a corresponding growth factor having improved secretion efficiency as compared to a wild-type growth factor, wherein the wild-type pro-neurotrophin has an asparagine residue at a position 4 amino acids upstream from the site of cleavage for the mature growth factor, the mutant pro-neurotrophin comprising a polypeptide in which the wild-type asparagine residue is replaced by a basic residue.
6. The mutant pro-neurotrophin according to Claim 5, wherein the basic residue is serine.
7. The mutant pro-neurotrophin according to Claim 5, wherein the corresponding neurotrophin is NT-4/5.
8. The mutant pro-neurotrophin according to Claim 5, wherein the polypeptide is a recombinant one, and the replacement of the wild-type asparagine is made by mutation of a polynucleotide encoding the wild-type pro-neurotrophin.
9. A mutant pro-neurotrophin precursor polypeptide selected from the group of polypeptides consisting of SEQ.ID.Nos. 1, 3, 5 and 7.
10. A mutant pro-neurotrophin comprising the precursor polypeptide of Claim 9 joined by a cleavage site to a corresponding mature growth factor.
11. A polynucleotide encoding a mutant pro-neurotrophin, wherein the polynucleotide differs in nucleotide sequence from wild-type by replacement of the codon encoding a target asparagine residue, at a position 8 amino acids upstream from the site of

cleavage for the corresponding growth factor, with a substitution codon encoding a basic residue.

12. The polynucleotide according to Claim 7, wherein the substitution codon encodes serine.
13. The polynucleotide according to Claim 7, wherein the corresponding neurotrophin is selected from the group consisting of NGF, NT-3 and BDNF.
14. The polynucleotide of SEQ.ID.No. 16.
15. A polynucleotide encoding a mutant pro-neurotrophin, wherein the polynucleotide differs in nucleotide sequence from wild-type by replacement of the codon encoding a target asparagine residue, at a position 4 amino acids upstream from the site of cleavage for the corresponding neurotrophin, with a substitution codon encoding a basic residue.
16. The polynucleotide according to Claim 15, wherein the substitution codon encodes serine.
17. The polynucleotide according to Claim 15, wherein the corresponding neurotrophin is NT-4/5.
18. A recombinant expression vector containing the polynucleotide of any of Claims 11, 14 or 15.
19. A host cell containing the recombinant expression vector of of any of Claims 11, 14 or 15.
20. A pharmaceutical composition comprising the recombinant expression vector of of any of Claims 11, 14 or 15.
21. A pharmaceutical composition comprising the host cell of any of Claims 11, 14 or 15.
22. A process for producing a mutant pro-neurotrophin for use in intracellular processing of a corresponding growth factor having improved secretion efficiency as compared to wild-type growth factor, the process comprising (a) synthesis of the mutant pro-neurotrophin encoding polynucleotide, wherein the polynucleotide differs in nucleotide sequence from wild-type by replacement of the codon encoding a target asparagine residue, at a position 8 amino acids upstream from the site of cleavage for the corresponding growth factor, with a substitution codon encoding a basic residue; and (b) causing the synthetic polynucleotide to express the pro-neurotrophin.
23. The process according to Claim 22, wherein the polynucleotide of Claims 11 or 14 is produced by step (a).

